

WHAT IS CLAIMED IS:

- 1 1. An isolated nucleic acid encoding a peptide comprising the amino acid sequence of SEQ
2 ID NO:2 or SEQ ID NO:2 with a conservative amino acid substitution.
- 1 2. The nucleic acid of Claim 1 wherein the peptide contains 25 to 35 amino acids.
- 1 3. The nucleic acid of Claim 2 comprising the nucleotide sequence of SEQ ID NO:1.
- 1 4. An isolated nucleic acid encoding a peptide comprising the amino acid sequence of SEQ
2 ID NO:4 or SEQ ID NO:4 with a conservative amino acid substitution.
- 1 5. An isolated nucleic acid encoding a peptide comprising the amino acid sequence of SEQ
2 ID NO:44 or SEQ ID NO:44 with a conservative amino acid substitution.
- 1 6. The nucleic acid of Claim 6 wherein the peptide contains 27 to 40 amino acids.
- 1 7. A nucleic acid encoding a peptide containing 7 to 100 amino acids comprising three
2 contiguous amino acids from the amino acid sequence of SEQ ID NO:2; and wherein the
3 peptide can stimulate the lysis of both wild type *pneumococci*, and a strain of *pneumococcus*
4 that is autolysin deficient.
- 1 8. The nucleic acid of Claim 7 wherein the peptide contains 12 to 50 amino acids.
- 1 9. The nucleic acid of Claim 8 wherein the peptide contains 17 to 35 amino acids.
- 1 10. A nucleic acid encoding a peptide containing 22 to 100 amino acids and comprising an
2 amino acid sequence of
3 RKEFHXXXXXXQLLXDKRPXRDY
4 or the amino acid sequence having a conservative amino acid substitution; wherein the
5 peptide can inhibit the growth or kill both wild type *pneumococci*, and a strain of
6 *pneumococcus* that is autolysin deficient.
- 1 11. A peptide comprising the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:2 with a
2 conservative amino acid substitution.

1 31. The method of Claim 29 further comprising:

2 (d) testing the peptide for its ability to inhibit the growth or kill a strain of a
3 bacterium that is deficient in an autolysin; wherein the peptide is identified when it can
4 inhibit the growth or kill both the wild type and the autolysin deficient strain of bacterium.

1 32. The method of Claim 29 wherein the bacterium is selected from the group consisting of
2 *Pneumococcus*, *Methanococcus*, *Haemophilus*, *Archaeoglobus*, *Borrelia*, and
3 *Syndedrocyptis*.

1 33. The peptide identified by the method of Claim 31.

1 34. A method of identifying an agent that is capable of inhibiting the growth of or killing a
2 bacterial cell comprising:

3 (a) contacting the agent with a bacterial cell, wherein the bacterial cell has a
4 defective His-Asp phosphorelay pathway; and

5 (b) determining whether the cell is killed or its growth is inhibited; wherein an agent
6 is identified as capable of killing or inhibiting the growth of a bacterial cell if it kills or
7 inhibits the growth of the bacterial cell.

1 ²35. The method of Claim ¹34 wherein the bacterial cell is a vancomycin tolerant cell.

1 ¹⁷36. The method of Claim ¹34 wherein the bacterial cell is not killed by a peptide having the
2 amino acid sequence of SEQ ID NO:2.

1 ⁸37. The method of Claim ¹34 wherein the bacterial cell is a *pneumococcal* cell.

1 ³38. The method of Claim ²35 wherein the His-Asp phosphorelay pathway lacks a functional
2 sensor histidine kinase having a wild type amino acid sequence of SEQ ID NO:14.

1 ⁵39. The method of Claim ²35 wherein the His-Asp phosphorelay pathway lacks a functional
2 response regulator having a wild type amino acid sequence of SEQ ID NO:16.

- 1 12. The peptide of Claim 11 wherein the peptide contains 25 to 35 amino acids.
- 1 13. A peptide comprising the amino acid sequence of SEQ ID NO:4 or SEQ ID NO:4 with a
2 conservative amino acid substitution.
- 1 14. The peptide of Claim 13 wherein the peptide contains 25 to 35 amino acids.
- 1 15. A peptide comprising the amino acid sequence of SEQ ID NO:44 or SEQ ID NO:44 with
2 a conservative amino acid substitution.
- 1 16. The peptide of Claim 15 wherein the peptide contains 27 to 40 amino acids.
- 1 17. A peptide containing 7 to 100 amino acids comprising three contiguous amino acids from
2 the amino acid sequence of SEQ ID NO:2; wherein the peptide can inhibit the growth or kill
3 both wild type *pneumococci*, and a strain of *pneumococcus* that is autolysin deficient.
- 1 18. The peptide of Claim 17 which contains 12 to 50 amino acids.
- 1 19. The peptide of Claim 18 which contains 17 to 35 amino acids.
- 1 20. A peptide containing 23 to 100 amino acids and comprising an amino acid sequence of
2 RKEFHXXXXXXQLLXDKRPXRDY
3 or the amino acid sequence having the conservative amino acid substitution; wherein the
4 peptide can inhibit the growth or kill both wild type *pneumococci*, and a strain of
5 *pneumococcus* that is autolysin deficient.
- 1 21. An antibody raised against the peptide of Claim 16.
- 1 22. The antibody of Claim 21 that is a monoclonal antibody.
- 1 23. An immortal cell line that produces a monoclonal antibody according to Claim 22.
- 1 24. A pharmaceutical composition for treating a bacterial infection comprising the peptide of
2 Claim 11 and a pharmaceutically acceptable carrier.

1 25. A method of identifying a peptide that can stimulate the lysis of a wild type strain of a
2 bacterium comprising
3 (a) locating an open reading frame in a gene cluster of a bacterial genome; wherein
4 the gene cluster encodes two or more components involved in the His-Asp phosphorelay
5 signal transduction system;
6 (b) making a peptide which is encoded by the open reading frame; and
7 (c) testing the peptide for its ability to inhibit the growth or kill a wild type strain of
8 a bacterium; wherein the peptide is identified when it can inhibit the growth or kill the
9 bacterium.

1 26. The method of Claim 25 further comprising:
2 (d) testing the peptide for its ability to inhibit the growth or kill a strain of a
3 bacterium that is deficient in an autolysin; wherein the peptide is identified when it can
4 inhibit the growth or kill both in the wild type and in the autolysin deficient strain of
5 bacterium.

1 27. The method of Claim 25 wherein the gene cluster encodes a transmembrane sensor
2 histidine kinase, and a response regulator.

1 28. The method of Claim 28 wherein the gene cluster further encodes an ABC transporter.

1 29. A method of identifying a peptide that can stimulate the lysis of a wild type strain of a
2 bacterium comprising:
3 (a) locating an open reading frame in a bacterial genome; wherein the open reading
4 frame is within one kilobase of a second open reading frame encoding an ABC transporter
5 complex;
6 (b) making a peptide which is encoded by the open reading frame; and
7 (c) testing the peptide for its ability to inhibit the growth or kill a wild type strain of
8 a bacterium; wherein the peptide is identified when it can inhibit the growth or kill the
9 bacterium.

1 30. The method of Claim 29 wherein the open reading frame is also within one kilobase of a
2 third open reading frame that encodes a component involved in the His-Asp phosphorelay
3 signal transduction system.

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- 1 40. A method of identifying an agent that is capable of inhibiting the growth of or killing a
2 bacterial cell comprising:
3 (a) contacting the agent with a bacterial cell, wherein the bacterial cell has a
4 defective ABC transporter system; and
5 (b) determining whether the cell is killed or its growth is inhibited; wherein an agent
6 is identified as capable of killing or inhibiting the growth of a bacterial cell if it kills or
7 inhibits the growth of the bacterial cell.
- 1 41. The method of Claim 40 wherein the bacterial cell is a vancomycin tolerant cell.
- 1 42. The method of Claim 40 wherein the bacterial cell is a *pneumococcal* cell.
- 1 43. The method of Claim 42 wherein the ABC transporter system lacks a functional
2 component having a wild type amino acid sequence selected from the group consisting of
3 SEQ ID NO:18, SEQ ID NO:20, and SEQ ID NO:22.
- 1 44. A cell that has been altered so as to have a defective His-Asp phosphorelay system;
2 wherein the cell is not killed by a peptide having the amino acid sequence of SEQ ID NO:2.
- 1 45. The cell of Claim 44 that is a bacterial cell.
- 1 46. The cell of Claim 45 wherein the cell is not killed by penicillin.
- 1 47. The bacterial cell of Claim 45 that is a vancomycin tolerant cell.
- 1 48. The bacterial cell of Claim 45 selected from the group of bacteria consisting of
2 *Pneumococcus*, *Methanococcus*, *Haemophilus*, *Archaeoglobus*, *Borrelia*, and
3 *Syndedrocyptis*.
- 1 49. The bacterial cell of Claim 48 wherein the bacterial cell is a *pneumococcal* cell.
- 1 50. The bacterial cell of Claim 49 wherein the His-Asp phosphorelay pathway lacks a
2 functional sensor histidine kinase having a wild type amino acid sequence of SEQ ID NO:14.

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1 51. The bacterial cell of Claim 49 wherein the His-Asp phosphorelay pathway lacks a
2 functional response regulator having a wild type amino acid sequence of SEQ ID NO:16.

1 52. A cell that has been altered so as to have a defective ABC transporter system;
2 wherein the cell is not killed by a peptide having the amino acid sequence of SEQ ID NO:2.

1 53. The cell of Claim 52 that is a bacterial cell.

1 54. The cell of Claim 53 wherein the cell is not killed by penicillin.

1 55. The bacterial cell of Claim 53 that is a vancomycin tolerant cell.

1 56. The bacterial cell of Claim 55 selected from the group of bacteria consisting of
2 *Pneumococcus*, *Methanococcus*, *Haemophilus*, *Archaeoglobus*, *Borrelia*, and
3 *Syndedrocyptis*.

1 57. The bacterial cell of Claim 56 wherein the bacterial cell is a *pneumococcal* cell.

1 58. The bacterial cell of Claim 57 wherein the ABC transporter system lacks a functional
2 component having a wild type amino acid sequence selected from the group consisting of
3 SEQ ID NO:18, SEQ ID NO:20, and SEQ ID NO:22.

1 59. A method of identifying a pneumococcal cell that contains a mutation in a
2 histidine kinase gene comprising:

3 (a) preparing a PCR amplification product for a nucleic acid using a primer for said
4 histidine kinase gene, wherein said nucleic acid is obtained from the pneumococcal cell; and

5 (b) comparing the PCR amplification product with a control amplification product
6 prepared using said primer and a control nucleic acid encoding the wild type amino acid
7 sequence of the histidine kinase; wherein the control nucleic acid encodes the amino acid
8 sequence of SEQ ID NO:14; and wherein when said comparing indicates a difference, the
9 pneumococcal cell is identified as containing a mutation in said histidine kinase gene.

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1 60. The method of Claim 59 wherein said comparing includes the evaluating of the PCR
2 amplification products by single strand conformation polymorphism.

1 61. The method of Claim 59 wherein the pneumococcal cell is a vancomycin tolerant cell.

1 62. A method of identifying a pneumococcal cell that contains a mutation in a
2 response regulator gene comprising:

3 (a) preparing a PCR amplification product for a nucleic acid using a primer for said
4 response regulator gene, wherein said nucleic acid is obtained from the pneumococcal cell;
5 and

6 (b) comparing the PCR amplification product with a control amplification product
7 prepared using said primer and a control nucleic acid encoding the wild type amino acid
8 sequence of the response regulator; wherein the control nucleic acid encodes the amino acid
9 sequence of SEQ ID NO:16; and wherein when said comparing indicates a difference, the
10 pneumococcal cell is identified as containing a mutation in said response regulator gene.

1 63. The method of Claim 62 wherein said comparing includes the evaluating of the PCR
2 amplification products by single strand conformation polymorphism.

1 64. The method of Claim 62 wherein the pneumococcal cell is a vancomycin tolerant cell.

1 65. A method of identifying a pneumococcal cell that contains a mutation in a gene for a
2 component of the ABC transporter comprising:

3 (a) preparing a PCR amplification product for a nucleic acid using a primer for said
4 component of the ABC transporter gene, wherein said nucleic acid is obtained from the
5 pneumococcal cell; and

6 (b) comparing the PCR amplification product with a control amplification product
7 prepared using said primer and a control nucleic acid encoding the wild type amino acid
8 sequence of the component of ABC transporter gene; wherein the control nucleic acid
9 encodes the amino acid sequence selected from the group consisting of SEQ ID NO:18, SEQ
10 ID NO: 20 and SEQ ID NO:22; and wherein when said comparing indicates a difference, the
11 pneumococcal cell is identified as containing a mutation in said component of the ABC
12 transporter gene.

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- 1 66. The method of Claim 65 wherein said comparing includes the evaluating of the PCR
- 2 amplification products by single strand conformation polymorphism.
- 1 67. The method of Claim 65 wherein the pneumococcal cell is a vancomycin tolerant cell.

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